

**REMARKS**

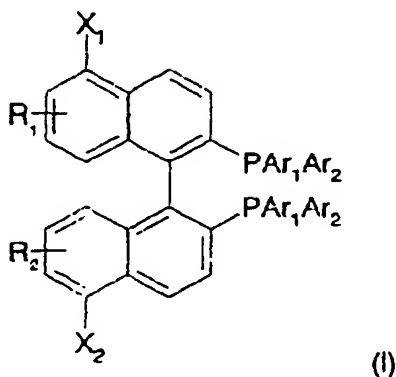
Claims 65-95 are all the claims pending in the present application.

Reconsideration of the application identified in caption in light of the following remarks is respectfully requested.

**I. Response to Rejection under 35 U.S.C. § 103(a)**

Claims 65-68, 94 and 95 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Lamouille et al., "Hydrogenation of ethyl acetoacetate catalyzed by hydrosoluble BINAP derivatives," Tetrahedron Letters (2001), 42(4), 663-664, Ter Hallea et al., "Synthesis and evaluation of poly-NAP-Ru, an heterogeneous enantioselective catalyst," Comptes Rendus de l'Academie des Sciences, Serie IIC: Chimie (2000), 3(7), 553-56, or WO 2000049028 (equivalent to U.S. Patent No. 6,610,875) to Lemaire et al. Applicants respectfully traverse the rejection for the reasons set forth in the Amendment filed January 7, 2008, and the following additional reasons.

Independent claim 65 recites a diphosphine in racemic form or in chiral form, corresponding to formula (I):



in said formula:

- $R_1$  and  $R_2$ , which are identical or different, represent a hydrogen atom or a substituent,
- $Ar_1$  and  $Ar_2$  independently represent an alkyl, alkenyl, cycloalkyl, aryl or arylalkyl group,
- $X_1$  and  $X_2$ , which are identical or different, represent:
  - an alkyl, alkenyl, alkynyl, cycloalkyl, aryl or arylalkyl group,
  - an alkyl group substituted with one or more halogen atoms, or with nitro or amino groups,
  - a halogen atom selected from the group consisting of bromine, chlorine and iodine,
  - an -OH group,
  - a group -O-COR<sub>a</sub>,
  - a group -O-R<sub>a</sub>,
  - a group -S-R<sub>a</sub>,
  - a -CN group,
  - a group selected from the group consisting of:
    - a -CH<sub>2</sub>-NH<sub>2</sub> group, and
    - a -COOH group,
  - a group selected from the group consisting of:
    - a group -COOR<sub>a</sub>,
    - a -CH<sub>2</sub>OH group, and
    - a group -CO-NH-R<sub>b</sub>,
  - a group selected from the group consisting of:
    - a group -CH<sub>2</sub>-NH-CO-R<sub>b</sub>,
    - a group -CH<sub>2</sub>-NH-CO-NH-R<sub>b</sub>,

a group  $-\text{CH}_2-\text{N}=\text{CH}-\text{R}_a$ ,

a  $-\text{CH}_2-\text{N}=\text{C}=\text{O}$  group, and

a  $-\text{CH}_2-\text{NH}_4^+$  group,

a group selected from the group consisting of:

a group  $-\text{N}=\text{CH}-\text{R}_a$ ,

an  $-\text{NH}-\text{NH}_2$  group,

an  $-\text{N}=\text{N}^+=\text{N}^-$  group, and

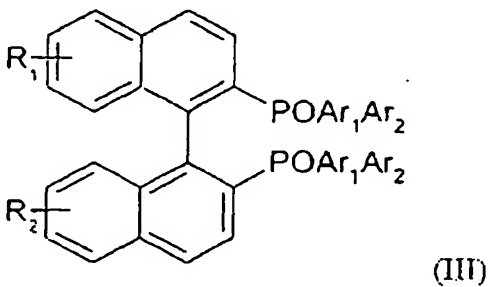
an  $-\text{N}=\text{C}=\text{O}$  group,

a magnesium or lithium atom,

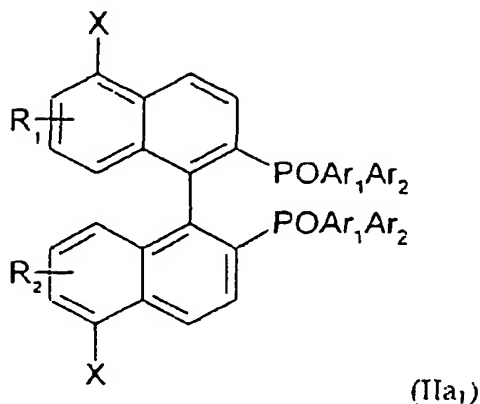
in the various formulae,  $\text{R}_a$  represents an alkyl, cycloalkyl, arylalkyl or phenyl group and  $\text{R}_b$  has the meaning given for  $\text{R}_a$  and also represents a naphthyl group.

As demonstrated in the examples of the present specification, the recited diphosphines can provide unexpectedly superior results in asymmetric catalysis, e.g., asymmetric hydrogenation. In particular, Example 5 having the ligands 5,5'-diamBINAP, and Examples 10 and 11 having the ligands 5,5'-perfluoroalkylBINAP showed e.e. of 99% in hydrogenation reactions.

The recited diphosphine can be prepared by a process comprising a step of halogenation in positions 5,5' of a compound of formula (III):



using a halogen and in the presence of iron, so as to obtain the corresponding dihalo compound of formula:



in said formula: X represents a chlorine, bromine or iodine atom.

The product (IIa<sub>1</sub>) resulting from this halogenation step is the starting material for the preparation of the recited diphosphines of formula (1). As set forth above, the halogenation in positions 5,5' of the above formula (III) is carried out by use of a halogen in the presence of iron.

Applicants wish to point out that the recited diphosphines are new and cannot be prepared by the methods described in the cited documents. Applicants now address the cited documents in the following three categories:

- Lemaire's work,
- U.S. Patent No. 5,274,146 to Ishizaki et al.,
- Fan et al., Tetrahedron Asymmetry, 12 (2001), 1241 -1247.

a. Lemaire's work

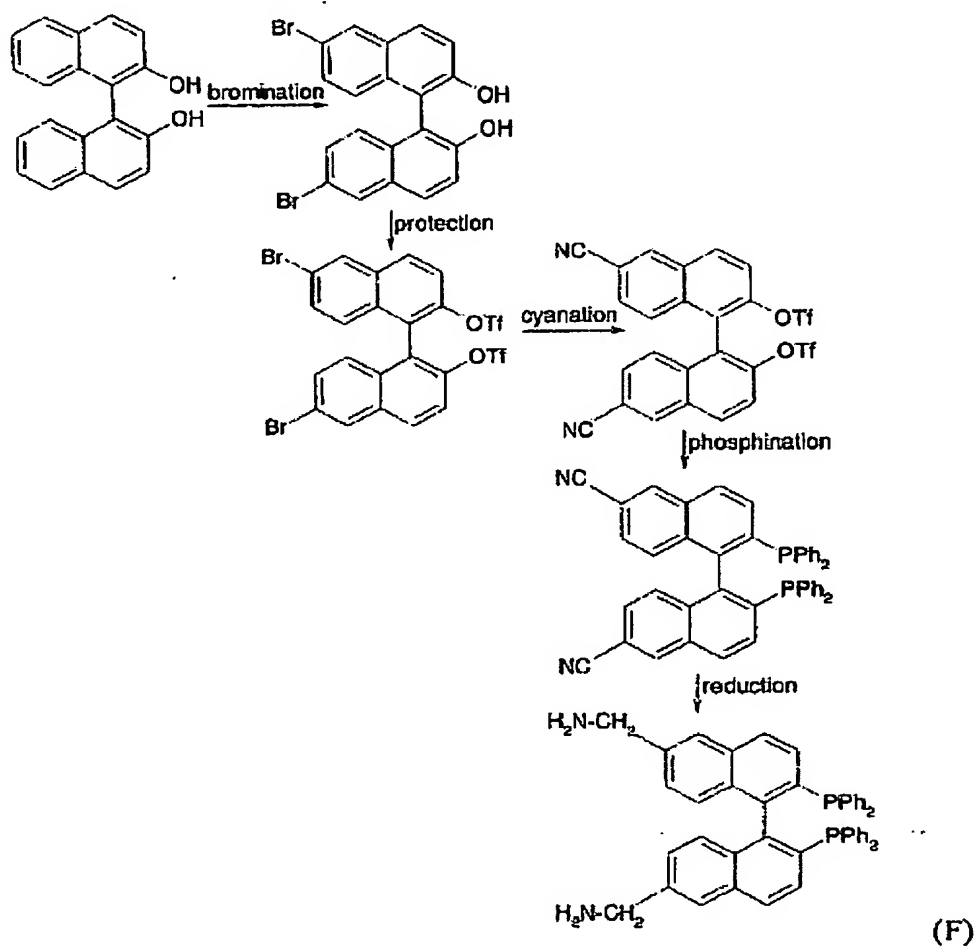
There are four (4) documents related to the Lemaire's studies:

- U.S. Patent No. 6,610,875,
- U.S. Patent No. 6,646,106,
- Hallea et al., CR Acad Sci Paris, 3 (2000), 553-556,

- Lamouille et al., Tetrahedron Letters, 42 (2001), 663-664.

Applicants wish to point out that the above mentioned patents were assigned to the assignee of the present application, Rhodia Chimie.

These documents relate to the following compound (F) with two aminomethyl groups in positions 6 and 6':

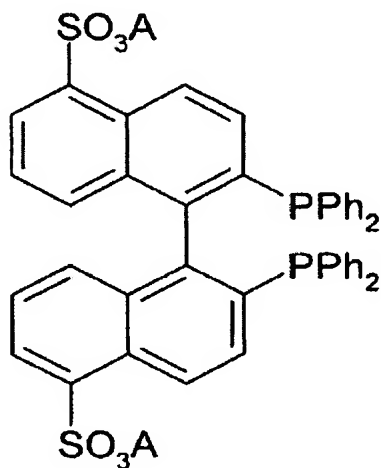


The halogenation is performed on a binol by the means of halogen + solvent. As shown in the above diagram, this halogenation reaction results in halogenation at positions

6,6', and not 5,5', of the binol. None of these documents disclose a process for the preparation of a diphosphine with two functional groups in positions 5 and 5'.

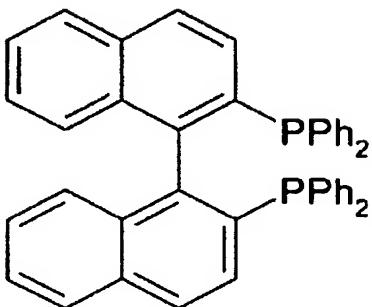
b. U.S. Patent No. 5,274,146 to Ishizaki et al.

Ishizaki et al. discloses an alkali metal sulfonate-substituted binaphthyl-phosphine of the following formula:



In this formula, the functional groups are in positions 5 and 5'. However, -SO<sub>3</sub>A group is not included in the definitions of X<sub>1</sub> and X<sub>2</sub> recited in present claim 65. Thus, this compound described in Ishizaki et al. is outside the scope of the present claims.

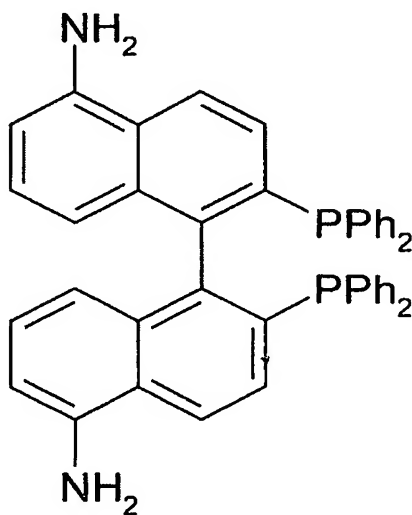
In Ishizaki et al., the alkali metal sulfonate-substituted binaphthyl-phosphine is prepared from sulfonation of BINAP with SO<sub>3</sub> - H<sub>2</sub>SO<sub>4</sub> (see the example):



Applicants advise that the process described in Ishizaki et al. cannot be used to prepare the 5,5'-substituted diphosphine recited in present claim 65.

c. Fan et al.

Fan et al. discloses a polymer prepared from the following diphosphine 5,5' diamino BINAP:



In this formula, the -NH<sub>2</sub> groups in positions 5 and 5' are not included in the definitions of X<sub>1</sub> and X<sub>2</sub> recited in present claim 65. Thus, this compound described in Fan et al. is outside the scope of the present claims.

The compound described in Fan et al. is a known product whose preparation process is particularly disclosed in U.S. Patent No. 4,705,895 cited in Fan et al. (ref. 19).

Specifically, the 5,5' diamino BINAP is prepared from reduction of 5,5' diamino BINAP dioxide which is prepared from reduction of 5,5' dinitro BINAP dioxide (see example 1).

Applicants advise that the process described in Fan et al. do not result in the 5,5'-substituted diphosphine recited in present claim 65.

In summary, none of the cited documents describe or suggest the diphosphines recited in present claim 65. Moreover, the presently recited diphosphines cannot be prepared in light of the teachings of the cited documents. Therefore, even if the cited documents are combined, the combination still would not result in the subject matter of present claim 65.

Furthermore, one of ordinary skill in the art seeking to provide diphosphines useful as ligands in the synthesis of catalysts based on transition metals, would not have been motivated to modify the ligands explicitly described in these cited documents, particularly, by replacing the substituents and/or locations thereof.

Additionally, as set forth above, the presently recited diphosphine can provide unexpectedly superior results in asymmetric catalysis, e.g., asymmetric hydrogenation. None of the cited documents disclose such feature. Applicants advise that in the field of asymmetric catalysis, it is not possible to predict the results including the enantioselectivity of a reaction.

In view of the foregoing, Applicants respectfully submit that claim 65 is patentable over the cited documents and thus the rejection should be withdrawn. Additionally, claims 66-69, 94 and 95 depend from claim 65, directly or indirectly, and thus are patentable over the cited documents at least by virtue of their dependency.

## **II. Response to Claim Objection**

Claim 74 was objected to as being dependent upon a rejected base claim.



Applicants respectfully submit that the rejection of claim 65, from which claim 74 depends, has been overcome as set forth above, and thus the objection should be withdrawn.


**III. Conclusion**

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited. If there are any questions concerning this paper or the application in general, the Examiner is invited to telephone the undersigned at (202) 452-7932 at his earliest convenience.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: September 30, 2008

By:   
Fang Liu, Ph.D.  
Registration No. 51283